

RECEIVED Cp. 1643  
JUN 20 2000

I hereby certify that this correspondence is being deposited with the United States Postal Services on the date set forth below as First Class Mail in an envelope addressed to: Commissioner for Patents, Washington, D.C. 20231.  
Date of Signature and Deposit: June 13, 2000

John C. Bahr  
Attorney of Record

#8  
JF  
8/23/00



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants: J. Drouin, et al.  
Serial No.: 09/319,782  
Filed: June 10, 1999  
For: NUR-RE A RESPONSE ELEMENT WHICH BINDS  
NUR NUCLEAR RECEPTORS AND METHOD OF  
USE THEREFOR  
Group Art Unit: --  
Examiner: --

Commissioner for Patents  
Washington, D.C. 20231

INFORMATION DISCLOSURE STATEMENT

Dear Sir:

Pursuant to 37 C.F.R. 1.98, enclosed herewith is a list of documents which the Applicants in the above-identified patent application wish to bring to the attention of the Examiner for consideration in connection with the examination on the merits of this patent application.

Foreign Patents

WO 95/28482; PCT; 26 October 1995.  
WO 96/21457; PCT; 18 July 1996.  
WO 96/29405; PCT; 26 September 1996

Other Documents

Dominic J. Autelitano, et al., "Corticotrope responsiveness to glucocorticoids is modulated via rapid

CRF-mediated induction of the proto-oncogene *c-fos*," *Mole. Cell. Endocrin.* 94:111-119, 1993.

20 2000  
TECH CENTER 1000, 1500

Miguel Beato, "Gene Regulation by Steroid Hormones," *Cell* 56:335-344, 1989.

Miguel Beato, *et al.*, "Steroid Hormone Receptors: Many Actors in Search of a Plot," *Cell* 83: 851-857, 1995.

A. L. Boutillier, *et al.*, "Corticotropin-Releasing Hormone Stimulates Proopiomelanocortin Transcription by *cFos*-Dependent and -Independent Pathways: Characterization of an AP1 Site in Exon 1," *Mole. Endocrin.* 9:745-755, 1995.

Barbara J. Calnan, *et al.*, "A Role for the Orphan Steroid Receptor Nur77 in Apoptosis Accompanying Antigen-Induced Negative Selection," *Immunity* 3:273-282, 1995.

R. K. W. Chan, *et al.*, "A Comparison of Two Immediate-Early Genes, *c-fos* and NGFI-B, as Markers for Functional Activation in Stress-related Neuroendocrine Circuitry," *J. Neuroscience* 13(12):5126-5138, 1993.

Ian J. Davis, *et al.*, "Endocrine and Neurogenic Regulation of the Orphan Nuclear Receptors Nur77 and Nurr-1 in the Adrenal Glands," *Mole. Cell. Biol.* 14:3469-3483, 1994.

Jacques Drouin, *et al.*, "Homodimer Formation Is Rate-Limiting for High Affinity DNA Binding by Glucocorticoid Receptor," *Mole. Endocrin.* 6:1299-1309, 1992.

Jacques Drouin, et al., "Novel glucocorticoid receptor complex with DNA element of the hormone-repressed POMC gene," EMBO J. 12:145-156, 1993.

Jacques Drouin, "Repression of transcription by nuclear receptors," Mech. Trans. Rep. pp. 118-140.

Jacques Drouin, et al., "Selective Effect of Androgens on LH and FSH Release in Anterior Pituitary Cells in Culture," Endo. 98:1528-1534, 1976.

Jacques Drouin, et al., "Structure of the rat pro-opiomelanocortin (POMC) gene," Fed. Eur. Biol. Soc. 193:54-58, 1985.

Barry Marc Forman, et al., "Unique Response Pathways Are Established by Allosteric Interactions among Nuclear Hormone Receptors," Cell 81:541-550, 1995.

Vincent Giguère, et al., "Determinants of Target Gene Specificity for ROR $\alpha$ 1: Monomeric DNA Binding by an Orphan Nuclear Receptor," Mole. Cell. Biol. 15:2517-2526, 1995.

Thomas G. Hazel, et al., "A gene inducible by serum growth factors encodes a member of the steroid and thyroid hormone receptor superfamily," Proc. Natl. Acad. Sci. USA 85:8444-8448, 1988.

Yoko Hirata, et al., "The Phosphorylation and DNA Binding of the DNA-binding Domain of the Orphan Nuclear Receptor NGFI-B\*," J. Biol. Chem. 268:24808-24812, 1993.

Jari Honkaniemi, et al., "Induction of multiple immediate early genes in rat hypothalamic paraventricular nucleus after stress," Mole. Brain Res. 25:234-241, 1994.

Lauren Jacobson, et al., "Regulation of Proopiomelanocortin Gene Transcription," Pit. Gland 2:117-138, 1994.

Carsten Jonat, et al., "Antitumor Promotion and Antiinflammation: Down-Modulation of AP-1 (Fos/Jun) Activity by Glucocorticoid Hormone," Cell 62:1189-1204, 1990.

Thomas Lamonerie, et al., "Ptx1, a *bicoid*-related homeo box transcription factor involved in transcription of the pro-opiomelanocortin gene," Genes & Dev. 10:1284-1295, 1996.

Simon W. Law, et al., "Identification of a New Brain-Specific Transcription Factor, NURR1," Mole. Endocrin. 6:2129-2135, 1992.

Zheng-Gang Liu, et al., "Apoptotic signals delivered through the T-cell receptor of a T-cell hybrid require the immediate-early gene *nur77*," Nature 367:281-284, 1994.

Mario Maira, et al., "Heterodimerization between Members of the Nur Subfamily of Orphan Nuclear Receptors as a Novel Mechanism for Gene Activation," Mole. Cell. Biol. 19:7549-7557, 1999.

David J. Mangelsdorf, et al., "The Nuclear Receptor Superfamily: The Second Decade," Cell 83:835-839, 1995.

David J. Mangelsdorf, et al., "The RXR Heterodimers and Orphan Receptors," Cell 83:841-850, 1995.

Jeffrey Milbrandt, "Nerve Growth Factor Induces a Gene Homologous to the Glucocorticoid Receptor Gene," Neuron 1:183-188, 1988.

Evelyn P. Murphy, et al., "Neuroendocrine Regulation of the Hypothalamic Pituitary Adrenal Axis by the nurrl/nur77 Subfamily of Nuclear Receptors," Mole. Endocrin. 16:39-47, 1997.

Akira Nakai, et al., "A Human Early Response Gene Homologous to Murine nur77 and Rat NGFI-B, and Related to the Nuclear Receptor Superfamily," Mole. Endocrin. 4:1438-1443, 1990.

Edward Oates, et al., "5' Sequence of Porcine and Rat Pro-opiomelanocortin mRNA," J. Biol. Chem. pp. 7421-7425, 1984.

Naganari Ohkura, et al., "Molecular Cloning of a Novel Thyroid/Steroid Receptor Superfamily Gene From Cultured Rat Neuronal Cells+," Biochem. Biophys. Res. Comm. 205:1959-1965, 1994.

David Parkes, et al., "Corticotropin-Releasing Factor Activates c-fos, NGFI-B, and Corticotropin-Releasing Factor Gene Expression within the Paraventricular Nucleus of the Rat Hypothalamus," Mole. Endocrin. 7:1357-1367, 1993.

Ragnhild E. Paulsen, et al., "Three Related Brain Nuclear Receptors, NGFI-B, Nurrl, and NOR-1, as Transcriptional Activators," J. Mole. Neur. 6:249-255, 1995.

Thomas Perlmann, et al., "A novel pathway for vitamin A signaling mediated by RXR heterodimerization with NGFI-B and NURR1," Genes & Dev. 9:769-782, 1995.

Alexandre Philips, et al., "Antagonism between Nur77 and Glucocorticoid Receptor for Control of Transcription," Mole. Cell. Biol. 17:5952-5959, 1997.

Alexandre Philips, et al., "Novel Dimeric Nur77 Signaling Mechanism in Endocrine and Lymphoid Cells," Mole. Cell. Biol. 17:5946-5951, 1997.

Anna Tate Riegel, et al., "Proopiomelanocortin Gene Promoter Elements Required for Constitutive and Glucocorticoid-Repressed Transcription," Mole. Endocrin. 5:1973-1982, 1991.

Rolf-Peter Ryseck, et al., "Structure, mapping and expression of a growth factor inducible gene encoding a putative nuclear hormonal binding receptor," EMBO J. 8:3327-3335, 1989.

Magdalena Schröder, et al., "Thyroid Hormone Receptor Functions as Monomeric Ligand-induced Transcription Factor on Octameric Half-sites," J. Biol. Chem. 269:6444-6449, 1994.

Roland Schüle, et al., "Functional Antagonism between Oncoprotein c-Jun and the Glucocorticoid Receptor," Cell 62:1217-1226, 1990.

Marc Therrien, et al., "Pituitary Pro-Opiomelanocortin Gene Expression Requires Synergistic Interactions of Several Regulatory Elements," Mole. Cell. Biol. 11:3492-3503, 1991.

Marc Therrien, et al., "Cell-Specific Helix-Loop-Helix Factor Required for Pituitary Expression of the Pro-Opiomelanocortin Gene," Mole. Cell. Biol. 13:2342-2353, 1993.

Thomas E. Wilson, et al., "The Orphan Receptors NGFI-B and Steroidogenic Factor 1 Establish Monomer Binding as a Third Paradigm of Nuclear Receptor-DNA Interaction," Mole. Cell. Biol. 13:5794-5804, 1993.

Thomas E. Wilson, et al., "Identification of the DNA Binding Site for NGFI-B by Genetic Selection in Yeast," Science 252:1296-1300, 1991.

Thomas E. Wilson, et al., "Participation of Non-Zinc Finger Residues in DNA Binding by Two Nuclear Orphan Receptors," Science 256:107-110, 1992.

Alan P. Wolfe, "Sinful Repression," Nature 387:16-17, 1997.

John D. Woronicz, et al., "Regulation of the Nur77 Orphan Steroid Receptor in Activation-Induced Apoptosis," Mole. Cell. Biol. 15:6364-6376, 1995.

John D. Woronicz, et al., "Requirement for the orphan steroid receptor Nur77 in apoptosis of T-cell hybridomas," Nature 367:277-281, 1994.

Hsin-Fang Yang-Yen, et al., "Transcriptional Interference between c-Jun and the Glucocorticoid Receptor: Mutual Inhibition of DNA Binding Due to Direct Protein-Protein Interaction," Cell 62:1205-1215, 1990.

Karina Yazdanbakhsh, et al., "Cyclosporin A blocks apoptosis by inhibiting the DNA binding activity of the

transcription factor Nur77," Proc. Natl. Acad. Sci. USA  
92:437-441, 1995.

No fee is believed necessary to enter this  
statement. However, if a fee is necessary please charge  
Deposit Account 17-0055.

Respectfully submitted,

J. Drouin, et al.

June 13, 2000

By: Jean C. Baker

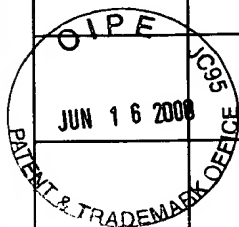
Jean C. Baker  
QUARLES & BRADY LLP  
411 East Wisconsin Avenue  
Milwaukee, WI 53202  
Reg. No.: 35,433  
(414) 277-5709







		✓	Ian Davis, <u>et al.</u> , "Endocrine and Neurogenic Regulation of the Orphan Nuclear Receptors Nur77 and Nurrl in the Adrenal Glands," <u>Mole. Cell. Biol.</u> 14:3469-3483, 1994.
		✓	Jacques Drouin, <u>et al.</u> , "Homodimer Formation Is Rate-Limiting for High Affinity DNA Binding by Glucocorticoid Receptor," <u>Mole. Endocrin.</u> 6:1299-1309, 1992.
		✓	Jacques Drouin, <u>et al.</u> , "Novel glucocorticoid receptor complex with DNA element of the hormone-repressed POMC gene," <u>EMBO J.</u> 12:145-156, 1993.
		✓	Jacques Drouin, "Repression of transcription by nuclear receptors," <u>Mech. Trans. Rep.</u> pp. 118-140.
		✓	Jacques Drouin, <u>et al.</u> , "Selective Effect of Androgens on LH and FSH Release in Anterior Pituitary Cells in Culture," <u>Endo.</u> 98:1528-1534, 1976.
		✓	Jacques Drouin, <u>et al.</u> , "Structure of the rat pro-opiomelanocortin (POMC) gene," <u>Fed. Eur. Biol. Soc.</u> 193:54-58, 1985.
		✓	Barry Marc Forman, <u>et al.</u> , "Unique Response Pathways Are Established by Allosteric Interactions among Nuclear Hormone Receptors," <u>Cell</u> 81:541-550, 1995.
		✓	Vincent Giguère, <u>et al.</u> , "Determinants of Target Gene Specificity for ROR $\alpha$ : Monomeric DNA Binding by an Orphan Nuclear Receptor," <u>Mole. Cell. Biol.</u> 15:2517-2526, 1995.
		✓	Thomas G. Hazel, <u>et al.</u> , "A gene inducible by serum growth factors encodes a member of the steroid and thyroid hormone receptor superfamily," <u>Proc. Natl. Acad. Sci. USA</u> 85:8444-8448, 1988.
		✓	Yoko Hirata, <u>et al.</u> , "The Phosphorylation and DNA Binding of the DNA-binding Domain of the Orphan Nuclear Receptor NGFI-B*," <u>J. Biol. Chem.</u> 268:24808-24812, 1993.
		✓	Jari Honkaniemi, <u>et al.</u> , "Induction of multiple immediate early genes in rat hypothalamic paraventricular nucleus after stress," <u>Mole. Brain Res.</u> 25:234-241, 1994.
		✓	Lauren Jacobson, <u>et al.</u> , "Regulation of Proopiomelanocortin Gene Transcription," <u>Pit. Gland</u> 2:117-138, 1994.
		✓	Carsten Jonat, <u>et al.</u> , "Antitumor Promotion and Antiinflammation: Down-Modulation of AP-1 (Fos/Jun) Activity by Glucocorticoid Hormone," <u>Cell</u> 62:1189-1204, 1990.
		✓	Thomas Lamonerie, <u>et al.</u> , "Ptx1, a bicoid-related homeo box transcription factor involved in transcription of the pro-opiomelanocortin gene," <u>Genes &amp; Dev.</u> 10:1284-1295, 1996.
		✓	Simon W. Law, <u>et al.</u> , "Identification of a New Brain-Specific Transcription Factor, NURR1," <u>Mole. Endocrin.</u> 6:2129-2135, 1992.
		✓	Zheng-Gang Liu, <u>et al.</u> , "Apoptotic signals delivered through the T-cell receptor of a T-cell hybrid require the immediate-early gene nur77," <u>Nature</u> 367:281-284, 1994.



		✓	Mar Maira, <u>et al.</u> , "Heterodimerization between Members of the Nur Subfamily of Orphan Nuclear Receptors as a Novel Mechanism for Gene Activation," <u>Mole. Cell. Biol.</u> 19:7549-7557, 1999.
		✓	David J. Mangelsdorf, <u>et al.</u> , "The Nuclear Receptor Superfamily: The Second Decade," <u>Cell</u> 83:835-839, 1995.
		✓	David J. Mangelsdorf, <u>et al.</u> , "The RXR Heterodimers and Orphan Receptors," <u>Cell</u> 83:841-850, 1995.
		✓	Jeffrey Milbrandt, "Nerve Growth Factor Induces a Gene Homologous to the Glucocorticoid Receptor Gene," <u>Neuron</u> 1:183-188, 1988.
		✓	Evelyn P. Murphy, <u>et al.</u> , "Neuroendocrine Regulation of the Hypothalamic Pituitary Adrenal Axis by the nurrl/nur77 Subfamily of Nuclear Receptors," <u>Mole. Endocrin.</u> 16:39-47, 1997.
		✓	Akira Nakai, <u>et al.</u> , "A Human Early Response Gene Homologous to Murine nur77 and Rat NGFI-B, and Related to the Nuclear Receptor Superfamily," <u>Mole. Endocrin.</u> 4:1438-1443, 1990.
		✓	Edward Oates, <u>et al.</u> , "5' Sequence of Porcine and Rat Pro-opiomelanocortin mRNA," <u>J. Biol. Chem.</u> pp. 7421-7425, 1984.
		✓	Naganari Ohkura, <u>et al.</u> , "Molecular Cloning of a Novel Thyroid/Steroid Receptor Superfamily Gene From Cultured Rat Neuronal Cells+," <u>Biochem. Biophys. Res. Comm.</u> 205:1959-1965, 1994.
		✓	David Parkes, <u>et al.</u> , "Corticotropin-Releasing Factor Activates c-fos, NGFI-B, and Corticotropin-Releasing Factor Gene Expression within the Paraventricular Nucleus of the Rat Hypothalamus," <u>Mole. Endocrin.</u> 7:1357-1367, 1993.
			Ragnhild E. Paulsen, <u>et al.</u> , "Three Related Brain Nuclear Receptors, NGFI-B, Nurrl, and NOR-1, as Transcriptional Activators," <u>J. Mole. Neur.</u> 6:249-255, 1995.
			Thomas Perlmann, <u>et al.</u> , "A novel pathway for vitamin A signaling mediated by RXR heterodimerization with NGFI-B and NURR1," <u>Genes &amp; Dev.</u> 9:769-782, 1995.
			Alexandre Philips, <u>et al.</u> , "Antagonism between Nur77 and Glucocorticoid Receptor for Control of Transcription," <u>Mole. Cell. Biol.</u> 17:5952-5959, 1997.
			Alexandre Philips, <u>et al.</u> , "Novel Dimeric Nur77 Signaling Mechanism in Endocrine and Lymphoid Cells," <u>Mole. Cell. Biol.</u> 17:5946-5951, 1997.
			Anna Tate Riegel, <u>et al.</u> , "Proopiomelanocortin Gene Promoter Elements Required for Constitutive and Glucocorticoid-Repressed Transcription," <u>Mole. Endocrin.</u> 5:1973-1982, 1991.
			Rolf-Peter Ryseck, <u>et al.</u> , "Structure, mapping and expression of a growth factor inducible gene encoding a putative nuclear hormonal binding receptor," <u>EMBO J.</u> 8:3327-3335, 1989.
			Magdalena Schröder, <u>et al.</u> , "Thyroid Hormone Receptor Functions as Monomeric Ligand-induced Transcription Factor on Octameric Half-sites," <u>J. Biol. Chem.</u> 269:6444-6449, 1994.



			Rol. Schüle, <u>et al.</u> , "Functional Antagonism between Onco Protein c-Jun and the Glucocorticoid Receptor," <u>Cell</u> 62:1217-1226, 1990.
			Marc Therrien, <u>et al.</u> , "Pituitary Pro-Opiomelanocortin Gene Expression Requires Synergistic Interactions of Several Regulatory Elements," <u>Mole. Cell. Biol.</u> 11:3492-3503, 1991.
			Marc Therrien, <u>et al.</u> , "Cell-Specific Helix-Loop-Helix Factor Required for Pituitary Expression of the Pro-Opiomelanocortin Gene," <u>Mole. Cell. Biol.</u> 13:2342-2353, 1993.
			Thomas E. Wilson, <u>et al.</u> , "The Orphan Receptors NGFI-B and Steroidogenic Factor 1 Establish Monomer Binding as a Third Paradigm of Nuclear Receptor-DNA Interaction," <u>Mole. Cell. Biol.</u> 13:5794-5804, 1993.
			Thomas E. Wilson, <u>et al.</u> , "Identification of the DNA Binding Site for NGFI-B by Genetic Selection in Yeast," <u>Science</u> 252: 1296-1300, 1991.
			Thomas E. Wilson, <u>et al.</u> , "Participation of Non-Zinc Finger Residues in DNA Binding by Two Nuclear Orphan Receptors," <u>Science</u> 256:107-110, 1992.
			Alan P. Wolfe, "Sinful Repression," <u>Nature</u> 387:16-17, 1997.
			John D. Woronicz, <u>et al.</u> , "Regulation of the Nur77 Orphan Steroid Receptor in Activation-Induced Apoptosis," <u>Mole. Cell. Biol.</u> 15:6364-6376, 1995.
			John D. Woronicz, <u>et al.</u> , "Requirement for the orphan steroid receptor Nur77 in apoptosis of T-cell hybridomas," <u>Nature</u> 367:277-281, 1994.
			Hsin-Fang Yang-Yen, <u>et al.</u> , "Transcriptional Interference between c-Jun and the Glucocorticoid Receptor: Mutual Inhibition of DNA Binding Due to Direct Protein-Protein Interaction," <u>Cell</u> 62:1205-1215, 1990.
			Karina Yazdanbakhsh, <u>et al.</u> , "Cyclosporin A blocks apoptosis by inhibiting the DNA binding activity of the transcription factor Nur77," <u>Proc. Natl. Acad. Sci. USA</u> 92:437-441, 1995.
EXAMINER			DATE CONSIDERED
<p>* EXAMINER: Initial if a citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.</p>			